BENZOAZACROWN ETHERS AND DIBENZODIAZACROWN ETHERS WITH PERIPHERAL

CHROMOPHORE GROUPS

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Arylazo derivatives of benzoaza- and dibenzodiazacrown ethers were obtained by diazo coupling of benzoaza- and dibenodiazacrown ethers with 4-nitrobenzenediazonium chloride. A chromophore effect is observed in the reaction of 13-(4-nitrophenylazo)-2,3,5,6,8,9-hexahydro-10H-benzo[k][1,4,7,10]trioxaazacyclododecene with lithium ions in an aqueous organic medium in the presence of tetramethylammonium hydroxide.

The synthesis of benzocrown ethers with peripheral chromophore groups is of interest in connection with the fact that the introduction of a chromophore label expands the possibilities of investigation of the reaction of crown ethers with metal ions [1, 2]. In the present communication we present data on the synthesis and study of the first representatives of azo derivatives of benzo- and dibenzodiazacrown ethers:



Starting dibenzodiazacrown ethers VI and VII were obtained by cyclization of III [3] with oxalic and diglycolic acid dichlorides [4] and subsequent reduction of the resulting IV and V with lithium aluminum hydride in tetrahydrofuran (THF) under the conditions in [5].

Compounds II, VIII, and IX were obtained by coupling of macroheterocycles I [6], VI, and VII with 4-nitrobenzenediazonium chloride. Diazo coupling was accomplished at pH 5-6 in tetramethylammonium acetate.

Data from the PMR and IR spectra of II and IV-IX confirm their structures (Tables 1 and 2). An AA'BB' spectrum of the protons of a p-disubstituted benzene ring is observed for II in d_6 -DMSO (Table 1). The protons of this ring are markedly deshielded because of the presence of two electron-acceptor substituents. The signal of the NH proton is found at weak field (7.3 ppm) and is overlapped by signals of the aromatic protons of the trisubstituted benzene ring, while the signals of the protons of the methylene groups close to the benzene ring are also shifted to weak field as compared with I [6]. The signal of an amide group at weak field at \sim 9 ppm is observed in the PMR spectra of solutions of IV and V in d_6 -DMSO (Table 1). The aromatic protons in the ortho position relative to the amide substituent (1- and 15-H) are deshielded significantly (\geq 0.5 ppm) as compared with the remaining aromatic protons; the deshielding increases by 0.25 ppm when the (-CH₂OCH₂--) fragment is introduced into V. The deshielding is due to the effect of the magnetic anisotropy of the C=O group. The

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TABLE 1. PMR Spectra of II and IV-IX

	δ, ppm*									
ound	NH	benzene ring protons	polyoxyethylene chain protons			nitrophenyl ring protons				
du			ArOCH2-CH2O-							
ပို			a	β	NHCOCH₂O	2′,6′-H2	3′,5-H2			
II	7,30 s	7,36 m (11,12-H ₂); 7,26 ^d (14-H)	4,32 m 3,97 m	u(2-H); u(3-H);		7,59 d	8,25 d			
			5,6 m (5,6-H 4,32 π 3.85 π	2); 1(8-H); 1(9-H)						
IV	9,01s	7,73 d $(1,15-H_2)$; 6,95-7,28 m $(2,3,4,12,13,14-H_2)$	4,23 m	3,67 m	·	-				
v	8,99 s	(2,3,1,12,10,14-16) 7,98 d $(1,15-H_2)$; 6,86—7,14 m	4,20m	3,80 m	4,28 s	—				
VI	4,75	(2,3,4,12,13,14+16) 6,506,95 m (1,2,3,4,12,13,14, 15-H ₈)	4,15 m	3,78m	3,39 s NHCH ₂ —CH ₂ —					
VII	4,72	6,536,96 m (1,2,3,4,12,13,14,	4,15 m	3,92 m	3,29 m 3,77 m	-				
VIII	_†	6,82 (1,15-H ₂); 7,58 d (2,14-H ₂);	4,24 m	3,78 m	3,67s	8,28 d	7,8 d			
IX	†	$7,41 d (4,12-H_2)$ $6,77 d (1,15-H_2); 7,59 (2,14-H_2);$ $7,38 d (4,12-H_2)$	4,20 m	3,75 m	3,32 m 3,75 m	8,33 d	7,9 d			
*The spectra of VI and VII were obtained from solutions in										

CDCl₃, while the spectra of the remaining compounds were obtained from solutions in d_6 -DMSO. The spectra of VIII and IX were measured at 100°C, the spectrum of II was obtained at 80°C, and the spectra of the remaining compounds were recorded at 30°C.

[†]Not observed because of proton exchange.

deshielding is due to the effect of the magnetic anisotropy of the C=O group. The deshielding of the 1- and 15-H aromatic protons is intensified as the length of the oxyethylene chain increases, and this constitutes evidence that these protons draw closer to the C=O group as the macroring becomes larger.

The slight shifts of the frequencies of the NH and C=O stretching vibrations on passing from solutions to the solid phase (Table 2) constitute evidence for the absence in the solid phase of the usual (for secondary amides) dimerization through intermolecular hydrogen bonds. The reason for this is evidently shielding of the NH groups located in the inner cavity of the macrocycles.

In the PMR spectra of solutions of VI and VII in d_6 -DMSO (Table 1) the signal of the NH proton lies at ~ 4.7 ppm. The signals of the aromatic protons form an ABCD spectrum that is similar to the AA'BB' spectrum of o-disubstituted benzenes with identical substituents and, upon the whole, are shifted 0.3-0.5 ppm to stronger field as compared with the aromatic protons of IV and V, which differ with respect to the less pronounced electron-donor character of the substituents. The size of the macroring of VI and VII does not have a substantial effect on the character of the PMR spectra (Table 1).

The appreciable differences in the NH vibrations in the IR spectra of VI and VII (Table 2) are evidently caused by the conformational peculiarities of these compounds due to the different degrees of conjugation of the unshared pair of electrons of the N atom with the π -electron system of the benzene ring. Thus only free NH groups — two narrow bands at 3440 and 3386 cm⁻¹ — are observed for VI in the solid phase. In the case of VII in the solid phase bands of stretching vibrations of NH groups linked by intermolecular hydrogen bonds are observed along with bands of free NH groups. These differences are equalized, although not completely, in solutions in CHCl₃: The frequencies vary from 3404 to 3422 cm⁻¹, and in individual cases the bands have shoulders and inflections.

The signal of an NH proton is not observed in the PMR spectra of solutions of VIII and IX in d_6 -DMSO (Table 1) because of exchange broadening. As usual, electron-acceptor substituents (NO₂, N=N) deshield the aromatic protons in the ortho positions relative to them. The position of the signals of the aromatic protons is retained unchanged on passing from dibenzodiazacrown ethers VI and VII to their bisazo derivatives VIII and IX (Table 1) and does not depend on the size of the macroring.

Com- pound	v, cm-1								
	N	н			c-o-c aliph				
	CHCl3	suspension	$C=O O \Gamma NO_2$	arom					
II	3358	3360	1516 m, 1504 m, 1338 s	1290 s 259 s	1194 m 1140 m 1096 s				
IV	3387	3390 m	1692 br s, 1688 br s 1680 br m	1257 s	1117 s				
v	3401	3403 w	1690 br s	1258 br m	1118 s				
VI	3408	3440, 3386		1246 br m	1128 br				
VII	3422, 3385 sh	3438 br m 3318 br s		1248 br m	1120 brs				
VIII		3400 sh 3389	1527 s, 1343 vs	1268 brm	1125 brs 1098 brs				
IX		3436	1520 m, 1336 m	1268 br m	1124 brs 1105 brs				

TABLE 2. IR Spectra of Suspensions of II and IV-IX in Mineral Oil and Hexachlorobutadiene

In the IR spectra of VIII and IX in the solid phase (Table 2) the bands of the NH stretching vibrations are shifted slightly as compared with the corresponding dibenzodiazacrown ethers VI and VII (Table 2). In the IR spectra of VIII and IX as compared with the spectra of VI and VII (Table 2) new intense bands of symmetrical stretching vibrations of the NO₂ group appear at \sim 1340 cm⁻¹, and the bands of C-O-C_{arom} asymmetrical stretching vibrations vibrations are shifted \sim 20 cm⁻¹ to the higher frequency side (to 1270 cm⁻¹).

Chelating agent II reacts with lithium ions in aqueous dimethylformamide (DMF) in the presence of tetramethylammonium hydroxide; a bathochromic shift of the absorption maximum from 390 nm to 510 nm is observed in the electronic spectra of this case. Under the experimental conditions the selectivity factors are 100 for K(I), Cs(I), and Rb(I), 50 for Na(I), 20 for Ca(II), and 5 for Mg(II). Verification of the effect of large amounts of sodium, potassium, rubidium, and cesium is hindered by the formation of precipitates. The selectivity of II with respect to lithium ions is probably explained by the maximal correspondence of the sizes of the macroring cavity and the lithium ion and the disparity between the size of the macroring cavity and the sizes of the other alkali metal ions.

Under similar conditions VIII and IX do not react with alkali metal ions with an attendant change in the color of the solutions.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a Varian XL-100-12 spectrometer (100 MHz) with tetramethylsilane as the internal standard. The IR spectra were recorded with a UR-20 spectrometer. The electronic spectra were recorded with a SF-4A spectrophotometer in 1- cm thick quartz cuvettes. The individuality of the compounds was monitored on Silufol UV-254.

<u>6,7,9,10,16,17,18,19-Octahydrodibenzo[h,n][1,4,7,10,13]trioxadiazacyclopentadecene-17,</u> <u>18-dione (IV).</u> Solutions of 7.21 g (25 mmole) of III in 225 ml of benzene and 3.17 g (25 mmole) of oxalyl chloride in 225 ml of benzene were added simultaneously to a mixture of 10 ml of pyridine and 40 ml of benzene, after which the reaction mixture was stirred at 20°C for 24 h. It was then filtered, and the solvent was removed from the filtrate by vacuum distillation. The precipitate was removed by filtration and reprecipitated from solution in chloroform by the addition of petroleum ether to give 4.6 g (54%) of IV with mp 173-175°C. Found: C 62.7; H 5.2; N 8.0%. C₁₈H₁₈N₂O₅. Calculated: C 62.9; H 5.3; N 8.2%.

<u>6,7,9,10,16,17,18,20,21,22-Decahydrodibenzo[h,q][1,4,7,13,10,16]tetraoxadiazacyclo-octadecene-17,21-dione (V).</u> This compound was similarly obtained from III and diglycolic acid dichloride. Workup of the reaction mixture gave 3.9 g (40%) of a product with mp 172-174°C (mp 171-174°C [7]).

6,7,9,10,16,17,18,19-Octahydrodibenzo[h,n][1,4,7,10,13]trioxadiazacyclopentadecene (VI). A suspension of 1.5 g (40 mmole) of lithium aluminum hydride in 150 ml of anhydrous tetrahydrofuran (THF) was added with stirring at 20°C in the course of 15 min in a stream of nitrogen to a solution of 2.74 g (8 mmole) of IV in 150 ml of anhydrous THF, after which the mixture was refluxed in a stream of nitrogen for 8 h. It was then cooled to 10°C, and the excess hydride was decomposed by the addition of 70 ml of THF-water (2:1). The mixture was filtered, the solvent was removed from the filtrate by distillation, and the precipitate was removed by filtration and reprecipitated from solution in hot acetone by the addition of water to give 1.9 g (77%) of VI with mp 161-162.5°C. Found: C 68.6; H 7.0; N 8.9%. $C_{18}H_{22}N_2O_3$. Calculated: C 68.7; H 7.0; N 8.9%.

<u>6,7,9,10,16,17,18,20,21,22-Decahydrodibenzo[h,q][1,4,7,13,10,16]tetraoxadiazacycloocta-</u> <u>decene (VII).</u> This compound was obtained by a procedure similar to that used to prepare VI. Workup of the reaction mixture gave 2 g (71%) of a product with mp 204-205°C (mp 203-204°C [5]).

<u>Benzoaza- and Dibenzodiazacrown Ethers with Peripheral Arylazo Groups (II, VIII, IX).</u> <u>General Procedure.</u> A solution of 0.21 g (3 mmole) of sodium nitrite in 3 ml of water was added to a cooled (to 0-5°C) solution of 0.42 g (3 mmole) of 4-nitroaniline in 3 ml of concentrated HCl and 3 ml of water. After 10 min, the solution of the diazonium salt was added with stirring to 3 mmole of the benzoazacrown ether or 1.5 mmole of the dibenzodiazacrown ether in 20 ml of acetic acid. During the diazo coupling reaction pH 5-6 was maintained by the addition of a solution of tetramethylammonium acetate. The precipitate was removed by filtration, washed with water, and dried.

 $\frac{13-(4-\text{Nitrophenylazo})-2,3,5,6,8,9-\text{hexahydro-10H-benzo}[k][1,4,7,10]\text{trioxaazacyclododecene}}{(II). Recrystallization of the product from ethanol gave 0.45 g (38%) of IIwith mp 95-97°C and Rf 0.87 (acetone). Found: C 58.0; H 5.4; N 15.1%. C₁₈H₂₀N₄O₅. Calculated: C 58.0; H 5.4: N 15.0%.$

 $\frac{3,13-\text{Bis}(4-\text{nitrophenylazo})-6,7,9,10,16,17,18,19-\text{octahydrodibenzo}[h,n][1,4,7,10,13]\text{trioxa-diazacyclopentadecene (VIII).} The product was reprecipitated twice from hot DMF by the addition of ethanol to give 0.1 g (11%) of VIII with mp >300° and Rf 0.85 [butanol-acetic acidwater (4:1:5)]. Found: C 56.8; H 4.5; N 18.1%. C₃₀H₂₈N₈O₇. Calculated: C 58.8; H 4.6; N 18.3%.$

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